

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

5

Applicant's or agent's file reference PU9843-PCT	FOR FURTHER ACTION		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP99/10123	International filing date (day/month/year) 20/12/1999	Priority date (day/month/year) 22/12/1998	
International Patent Classification (IPC) or national classification and IPC C07K14/765			
Applicant AMERSHAM PHARMACIA BIOTECH AB et al.			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I Basis of the report
- II Priority
- III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV Lack of unity of invention
- V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI Certain documents cited
- VII Certain defects in the international application
- VIII Certain observations on the international application

Date of submission of the demand 19/07/2000	Date of completion of this report 22.03.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Kalsner, I Telephone No. +49 89 2399 8708



INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

International application No. PCT/EP99/10123

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17.)*):

Description, pages:

1-15 as originally filed

Claims, No.:

1-10 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages: ----
- the claims, Nos.:
- the drawings, sheets:

5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

International application No. PCT/EP99/10123

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims 1-8
	No:	Claims 9, 10
Inventive step (IS)	Yes:	Claims 3
	No:	Claims 1, 2, 4-8
Industrial applicability (IA)	Yes:	Claims 1-10
	No:	Claims

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP99/10123

**Ad Section V: Reason d statement with regard to novelty, inventive step or
industrial applicability**

1) Documents

D1...WO-A-98 08603

2) Novelty

2.1) **Claims 9 and 10** do not meet the requirements of Art. 33(2) PCT for the following reasons:

D1 describes experiments performed in order to determine the efficiency of different ligands (such as, e.g., 2-mercapto benzthiazol) to bind bovine serum albumin (p. 66-68).

Claims 9 and 10, which are directed to a method for screening for ligand structures that selectively bind serum albumin, are thus not considered novel over D1.

2.1) **Claims 1-8** are considered to meet the requirements of Art. 33(2) PCT.

Claim 1 relates to a method for selectively enriching/removing a serum albumin from a mixture of other compounds by contacting said mixture with a ligand of the formula specified in claim 1.

As a method for selectively enriching/removing a serum albumin from a mixture of other compounds as defined in claim 1 is not disclosed as such in the available prior art **claim 1** and claims dependent thereon (**claims 2-8**) are considered to meet the requirements of Art. 33(2) PCT.

3) Inventive step

Claims 1, 2 and 4-8 do not meet the requirements of Art. 33(3) PCT for the following reasons:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP99/10123

D1 is considered to represent the closest prior art. D1 discloses methods for isolating immunoglobulins using bicyclic aromatic or heteroaromatic ligand coupled to solid phase matrices. Furthermore, as mentioned above, experiments are disclosed which show the binding of serum albumin to some of these ligands.

It appears thus obvious for the skilled person when confronted with the problem of selectively removing/enriching serum albumin from a mixture, to apply the teaching of D1 in order to isolate serum albumin from a mixture of other components.

A method for selectively enriching/removing serum albumin from a mixture of other compounds by contacting said mixture with a ligand as defined in **claims 1, 2, 4, 5 and 7** is thus not considered to involve an inventive step.

Claim 3 which further defines the ligand X used in the method of claim 1 is considered to meet the requirements of Art. 33(3) PCT as these specific features of the method are not disclosed or suggested in the available prior art.

Ad Section VIII: Certain observations on the international application

Claim 1 does not meet the requirements of Art. 5 and 6 PCT for the following reasons:

According to the description (p. 14) not all of the 14 tested compounds seemed to specifically bind albumin. In view of these results it seems questionable that all possible compounds encompassed in claim 1 actually are useful for selectively enrich/remove serum albumin from a mixture of other compounds. The breadth of claim 1 thus appears unjustified. Hence, **claim 1** is objected under Art. 5 and 6 PCT.

PATENT COOPERATION TREA

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference PU9843	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/EP 99/ 10123	International filing date (day/month/year) 20/12/1999	(Earliest) Priority Date (day/month/year) 22/12/1998
Applicant AMERSHAM PHARMACIA BIOTECH AB et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 2 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing :

contained in the international application in written form.

filed together with the international application in computer readable form.

furnished subsequently to this Authority in written form.

furnished subsequently to this Authority in computer readable form.

the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. Certain claims were found unsearchable (See Box I).

3. Unity of Invention is lacking (see Box II).

4. With regard to the title,

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

5. With regard to the abstract,

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

as suggested by the applicant.

because the applicant failed to suggest a figure.

because this figure better characterizes the invention.

None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 99/10123

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/765

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 98 08603 A (UPFRONT CHROMATOGRAPHY A/S) 5 March 1998 (1998-03-05) cited in the application page 55	1-8
A	WO 96 02573 A (GIST-BROCADES) 1 February 1996 (1996-02-01) cited in the application the whole document	1-8
T	WO 99 33860 A (AMERSHAM PHARMACIA BIOTECH AB) 8 July 1999 (1999-07-08) the whole document	1-10



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the International filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the International filing date but later than the priority date claimed

- *T* later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the International search

18 May 2000

Date of mailing of the International search report

25/05/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5018 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Masturzo, P

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 99/10123

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9808603	A 05-03-1998	AU 4112397 A EP 0921855 A		19-03-1998 16-06-1999
WO 9602573	A 01-02-1996	AU 2989495 A CA 2195202 A EP 0773961 A JP 10504289 T		16-02-1996 01-02-1996 21-05-1997 28-04-1998
WO 9933860	A 08-07-1999	US 5994507 A AU 2083499 A		30-11-1999 19-07-1999

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

by and post

PCT

BF

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

(PCT Rule 71.1)

To: ROLLINS, Anthony John NYCOMED AMERSHAM PLC White Lion Road Amersham, Bucks HP7 9LL GRANDE BRETAGNE FAX NO. +44 1494 543977	PCT	
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Applicant's or agent's file reference PU9843-PCT	Date of mailing (day/month/year) 22.03.2001	
International application No. PCT/EP99/10123	International filing date (day/month/year) 20/12/1999	Priority date (day/month/year) 22/12/1998
Applicant AMERSHAM PHARMACIA BIOTECH AB et al.		

<ol style="list-style-type: none"> 1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application. 2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices. 3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices. <p>4. REMINDER</p> <p>The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).</p> <p>Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.</p> <p>For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.</p>	
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Name and mailing address of the IPEA/ European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx. 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Büchler, S Tel. +49 89 2399-8090	
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PU9843-PCT	FOR FURTHER ACTION		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP99/10123	International filing date (day/month/year) 20/12/1999	Priority date (day/month/year) 22/12/1998	
International Patent Classification (IPC) or national classification and IPC C07K14/765			
Applicant AMERSHAM PHARMACIA BIOTECH AB et al.			

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- IV Lack of unity of invention
- V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI Certain documents cited
- VII Certain defects in the international application
- VIII Certain observations on the international application

Date of submission of the demand 19/07/2000	Date of completion of this report 22.03.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Kalsner, I Telephone No. +49 89 2399 8708



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP99/10123

I. Basis of the report

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Description, pages:

1-15 as originally filed

Claims, No.:

1-10 as originally filed

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4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:
- the drawings, sheets:

5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP99/10123

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims 1-8
	No: Claims 9, 10
Inventive step (IS)	Yes: Claims 3
	No: Claims 1, 2, 4-8
Industrial applicability (IA)	Yes: Claims 1-10
	No: Claims

2. Citations and explanations
*see separate sheet***VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP99/10123

**Ad Section V: Reasoned statement with regard to novelty, inventive step or
industrial applicability****1) Documents**

D1...WO-A-98 08603

2) Novelty

2.1) **Claims 9 and 10** do not meet the requirements of Art. 33(2) PCT for the following reasons:

D1 describes experiments performed in order to determine the efficiency of different ligands (such as, e.g., 2-mercapto benzthiazol) to bind bovine serum albumin (p. 66-68).

Claims 9 and 10, which are directed to a method for screening for ligand structures that selectively bind serum albumin, are thus not considered novel over D1.

2.1) **Claims 1-8** are considered to meet the requirements of Art. 33(2) PCT.

Claim 1 relates to a method for selectively enriching/removing a serum albumin from a mixture of other compounds by contacting said mixture with a ligand of the formula specified in claim 1.

As a method for selectively enriching/removing a serum albumin from a mixture of other compounds as defined in claim 1 is not disclosed as such in the available prior art **claim 1** and claims dependent thereon (**claims 2-8**) are considered to meet the requirements of Art. 33(2) PCT.

3) Inventive step

Claims 1, 2 and 4-8 do not meet the requirements of Art. 33(3) PCT for the following reasons:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP99/10123

D1 is considered to represent the closest prior art. D1 discloses methods for isolating immunoglobulins using bicyclic aromatic or heteroaromatic ligand coupled to solid phase matrices. Furthermore, as mentioned above, experiments are disclosed which show the binding of serum albumin to some of these ligands.

It appears thus obvious for the skilled person when confronted with the problem of selectively removing/enriching serum albumin from a mixture, to apply the teaching of D1 in order to isolate serum albumin from a mixture of other components.

○ A method for selectively enriching/removing serum albumin from a mixture of other compounds by contacting said mixture with a ligand as defined in **claims 1, 2, 4, 5 and 7** is thus not considered to involve an inventive step.

Claim 3 which further defines the ligand X used in the method of claim 1 is considered to meet the requirements of Art. 33(3) PCT as these specific features of the method are not disclosed or suggested in the available prior art.

Ad Section VIII: Certain observations on the international application

Claim 1 does not meet the requirements of Art. 5 and 6 PCT for the following reasons:

⊕ According to the description (p. 14) not all of the 14 tested compounds seemed to specifically bind albumin. In view of these results it seems questionable that all possible compounds encompassed in claim 1 actually are useful for selectively enrich/remove serum albumin from a mixture of other compounds. The breadth of claim 1 thus appears unjustified. Hence, **claim 1** is objected under Art. 5 and 6 PCT.